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Original Research Article

Evaluation of vitamin D levels in term pregnancy and its obstetric outcome in Indian women

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ABSTRACT

Background: Vitamin D deficiency is currently a global pandemic affecting all age groups. Vitamin D is considered a fundamental hormone in calcium homeostasis and bone health. Risk of vitamin D deficiency increases during pregnancy due to increased maternal and fetal demands and altered vitamin D metabolism. Recently, maternal vitamin D deficiency has been linked to adverse pregnancy outcomes, including preeclampsia, gestational diabetes, fetal growth restriction and preterm birth. Adequate vitamin D status appears to be relevant to health at all ages, and even in prenatal life.

Methods: This is a cross sectional, observational study conducted in the department of obstetrics and gynaecology at R. L. Jalappa Hospital. A total number of 160 subjects were included. 5 ml of venous blood was collected and was centrifuged at 3000 rpm and stored at - 80°C till analysis. Analysis of 25-hydroxy Vitamin D was done using ELISA. **Results:** Majority of the subjects were vitamin D deficient (81.87%) and 12.5% were vitamin D insufficient and only 5.63% were vitamin D sufficient. The prevalence of vitamin D deficiency was more among primigravidas (85.6%) and was associated with higher rates of caesarean section (92.4%). High prevalence of vitamin D deficiency was seen in lower middle socioeconomic class (62.5%). Maternal vitamin D deficiency was associated low birth weight of neonates (100%).

Conclusions: In this study it was concluded that majority of subjects were vitamin D deficient and belonged to lower middle socioeconomic class. Majority of this subjects who underwent caesarean section were vitamin D deficient. Vitamin D deficiency was associated only with low birth weight of neonates and no other adverse obstetric outcome.

Keywords: Obstetric outcome, Term gestation, Vitamin D

INTRODUCTION

Vitamin D is considered a fundamental hormone in calcium homeostasis and bone health. It important role in cellular proliferation and differentiation, vascular function and immune regulation has been brought to light.¹ Recently, maternal vitamin D deficiency has been linked to adverse pregnancy outcomes, including preeclampsia, gestational diabetes, fetal growth

restriction and preterm birth. Adequate vitamin D status appears to be relevant to health at all ages, and even in prenatal life.²

Vitamin D is called calciferol and has 2 physiologically active forms - D2 (ergocalciferol) and D3 (cholecalciferol). Vitamin D3 is three times more effective in raising and maintaining serum concentrations of vitamin D.^{3,4}

Vitamin D2 and D3 are first metabolised in the liver to 25 (OH)D - calcidiol D2 and then in the kidneys to 1,25(OH)2 D - calcitriol D3 which is the active form responsible for calcium homeostasis and bone mineralisation.

Vitamin D status is affected by factors that regulate its production in the skin such as skin pigmentation, latitude, dressing codes, season, aging, obesity, sunscreen use, and air pollution and also by factors affecting its absorption or metabolism.⁵

Assessment of vitamin D status is done by 25(OH)D, as it reflects the sum total of vitamin D produced cutaneously and that obtained by food and supplements.

Objectives

- To estimate serum vitamin D levels in term pregnancy
- To determine the association between serum vitamin D levels in term pregnancy and its obstetric outcome.

METHODS

This is a cross sectional, observational study conducted in department of obstetrics and gynaecology, R. L. Jalappa Hospital and Research Center from December 2015 to March 2017.

A total number of 160 subjects were included. Under aseptic precautions 5ml of venous blood was collected. The sample was centrifuged at 3000 rpm and stored at -80°C till analysis. Analysis of 25-hydroxy vitamin D was done using ELISA.

Inclusion criteria

• All Singleton pregnant women between 37 to 40 weeks of gestation who came to Sri R. L. Jalappa Hospital and Research Centre during the study period.

Exclusion criteria

Pregnant women with-

- Multiple gestation
- Premature rupture of membranes
- Preterm labor
- Uterine anomalies
- Previous caesarean section
- Preexisting medical illness like hypertension, diabetes mellitus, cardiac disorders, renal diseases.
- Chronic granuloma forming conditions like sarcoidosis.
- On treatment with anticonvulsant, antifungal and anti-retroviral drugs.

The Results were calculated using the formula:

$$y = mx + c$$

Where, m = -0.0141 and c = 1.9001, y = -0.0141x + 1.9001

Vitamin D values was categorised according to the reference range of Endocrine society 2011.⁶

Vitamin D deficiency is defined as serum vitamin D concentration of less than 20 ng/ml, insufficiency as 21-29 ng/ml, sufficiency as more than 30 ng/ml and intoxication as more than 150 ng/ml.

Statistical analysis

Chi square test was used to test statistical significance.

P value <0.05 was considered statistically significant.

RESULTS

This prospective study was conducted in the Department of Obstetrics and Gynecology, R. L. Jalapa Hospital, attached to Sri Devraj Urs Medical College, Tamaka, Kolar, Karnataka.

A total number of 160 samples were collected and serum vitamin D levels were analysed.

Table 1: Serum vitamin D levels in term pregnancy.

Vitamin D status	Number of subjects N = 160	%
Deficiency (< 20 ng/ml)	131	81.87
Insufficiency (21-29 ng/ml)	20	12.50
Sufficiency (> 30 ng/ml)	9	5.63
Intoxication (> 150 ng/ml)	0	0

Out of the 160 subjects studied, 131 (81.98%) were having serum vitamin D level less than 20 ng/ml and none of them had serum vitamin D level above 150 ng/ml. Mean vitamin D level was 11.22 ng/ml at 95% Confidence interval for vitamin D (11.23 ± 1.89) (Table 1).

A total of 52.5% of subjects were in 23-28 years age group, 20.6% of subjects were in 18-22yrs age group, 18.1% were in 29-33 years age group, 8.8% were in 34-40 years age group. There was no statistically significant association found between age group and vitamin D level (Figure 1).

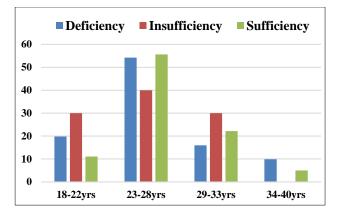


Figure 1: Distribution of subject according to age group and vitamin D level.

85.5

11.5

2.3

0.8

17

3

0

0

Pari

Primigravida

Gravida 2

Gravida 3

Gravida 4

112

15

3

1

A total 85.6% of subjects were primigravida, 11.6% of subjects were gravida 2, 1.9% were gravida 3, and only 0.6% were gravida 4.

There was no statistically significant association found between parity and vitamin D level (Table 2).

There was no statistically significant difference found between period of gestation and vitamin D level (Figure 2).

A total 92.5% of subjects had BMI in normal range, 5.6% of subjects were underweight and 1.9% of subjects were overweight.

value

0.982

	Vitamin D								
ity	Deficiency (N =	= 131)	Insufficienc	y (N = 20)	Sufficie	ncy (N = 9)	Total ((N = 160)	P-v
	No.	%	No.	%	No.	%	No.	%	

8

1

0

0

85

15

_

_

Table 2: Distribution of subjects is according to parity and vitamin D level.

Deficiency	Insufficiency	Sufficiency
50		
15		
0		
5		
0		
5		
0		
5		
0		
5		
0 37 - 37+6	38 - 38+6 39 -	39+6 40 - 40+6

Figure 2: Distribution of subjects according to period of gestation and vitamin D level.

There was no statistically significant difference found between BMI and vitamin D level (Table 3).

137

19

3

1

85.6

11.9

1.9

0.6

88.9

11.1

_

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In the total study population, 62.5% of subjects were in lower middle class, 18.8% in middle class, 13.8% in lower middle and 5% in lower class.

Of the vitamin D deficient subjects, 72.5% were in lower middle class. 65.0% of vitamin D insufficiency subject were in middle class. 77.8% of vitamin D sufficiency subject were in upper middle. There was a statistically significant association (<0.001) found between socioeconomic status and vitamin D level (Table 4).

A total 47.5% of subjects had studied up to primary school, 43.1% of subjects had studied up to high school, 6.3% of subjects were uneducated and only 3.1% of subjects were graduates.

	Vitamin D								
BMI	Deficiency (N = 131)		Insufficiency (N = 20)		Sufficiency $(N = 9)$		Total (N	Total (N = 160)	
	No.	%	No.	%	No.	%	No.	%	value
Underweight < 18.5	7	5.3	2	10	0	-	9	5.6	
Normal 18.5-24.99	121	92.4	18	90	9	100	148	92.5	0.747
Overweight > 25	3	2.3	0	-	0	-	3	1.9	

Table 3: Distribution of subjects is according to BMI and vitamin D level.

	Vitan	Vitamin D									
SE status	Defici	iency (N = 131)	Insufficie	Insufficiency (N = 20)		Sufficiency (N = 9)		Total (N = 160)			
	No.	%	No.	%	No.	%	No.	%	value		
Upper middle	0	-	1	5	7	77.8	8	5			
Middle class	15	11.5	13	65	2	22.2	30	18.8	< 0.001		
Lower middle	95	72.5	5	25	0	-	100	62.5	< 0.001		
Lower class	21	16	1	5	0	-	22	13.8			



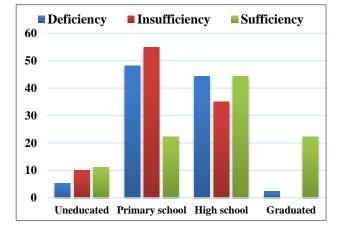


Figure 3: Distribution of subjects according to education status and vitamin D level.

There was no statistically significant difference found between education status and vitamin D level (Figure 3).

A total 70% of vitamin D insufficiency subjects had vaginal delivery, 88.9% of vitamin D sufficiency subjects had vaginal delivery and only 7.6% of vitamin D deficiency subjects had vaginal delivery rest 92.4% of vitamin D deficiency subjects underwent LSCS.

There was a statistically significant association (< 0.001) found between mode of delivery and vitamin D level (Figure 4).

Of the vitamin D deficient subjects who underwent LSCS, 61.8% had fetal distress, 13.7% had non progression of labour, 3.8% had placenta previa and

another 3.8% had malpresentation and 16.7% had maternal medical disease.

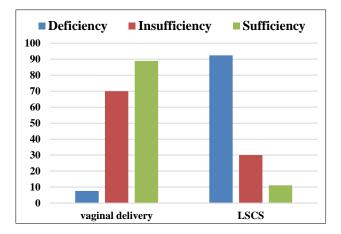


Figure 4: Distribution of subjects according to mode of delivery and vitamin D level.

There was a statistically significant association between indication for LSCS and vitamin D levels (p = 0.001) (Table 5).

Among 160 new-born babies, 25 new-born babies were LBW (1.5-2.5 kg), 127 babies were normal birth weight (2.5-3.5 kg) and eight babies were > 3.5 kg. All the mothers of 25 LBW babies had vitamin D deficiency (100%).

There was a statistically significant association (<0.001) found between birth weight and vitamin D level in mothers (Table 6).

Table 5: Distribution of subjects is according to indication for LSCS and vitamin D level.

Indication for LSCS	Vitam Deficio (N = 1	ency	Insuffic (N = 20)	•	Sufficie (N = 9)	ency	Total (N = 1	60)	P- value
	No.	%	No.	%	No.	%	No.	%	
Fetal distress	81	61.8	12	6	4	44.4	97	60.6	
Nonprogression of labour	18	13.7	4	2	1	11.1	23	14.3	
Placenta previa	5	3.8	1	0.5	3	33.3	9	5.6	< 0.001
Malpresentation	5	3.8	3	2.2	1	11.1	9	5.6	
Maternal medical disease	22	16.7	0	-	0	-	22	13.7	

D!41	Vitami	n D							
Birth	Deficiency (N = 131)		Insuff	Insufficiency (N = 20)		Sufficiency $(N = 9)$		(N = 160)	P-value
weight	No.	%	No.	%	No.	%	No.	%	
1.5-2.5 kg	25	19.1	0	-	0	-	25	15.6	
2.6-3.5 kg	105	80.2	17	85	5	55.6	127	79.4	< 0.001
> 3.5 kg	1	0.8	3	15	4	44.4	8	5	

Table 6: Distribution of subjects is according to birth weight and vitamin D level in mothers.

Table 7: Distribution of subjects is according to NICU admission of baby and vitamin D level in mothers.

NICII	Vitam	Vitamin D									
NICU admission	Deficie	ency (N = 131)	Insuffic	tiency (N = 20)	Suffici	ency (N = 9)	Total (N = 160)	P-value		
aumission	No.	%	No.	%	No.	%	No.	%			
Yes	14	10.7	1	5	1	11.1	16	10	0.727		
No	117	89.3	19	95	8	88.9	144	90	0.727		

Table 8: Distribution of subjects is according to neonatal complication and vitamin D level in mothers.

Nacrotal	Vitami	Vitamin D										
Neonatal complication	Deficiency (N = 131)		Insuffi	Insufficiency $(N = 20)$		Sufficiency (N = 9)		(N = 160)	P-value			
complication	No.	%	No.	%	No.	%	No.	%				
NIL	116	88.5	19	95	8	88.9	143	89.4				
SGA	2	1.5	0	-	0	-	2	1.3				
IUGR	3	2.3	0	-	0	-	3	1.9	0.959			
Respiratory distress	10	7.6	1	5	1	11.1	12	7.5				

Table 9: Distribution of subjects is according to maternal complication and vitamin D level.

Maternal	Vitam	Vitamin D										
complication	Deficiency (N = 131)		Insuffi	Insufficiency (N = 20)		Sufficiency $(N = 9)$		(N = 160)	P-value			
complication	No.	%	No.	%	No.	%	No.	%				
NIL	103	78.6	17	85	9	100	129	80.6				
PE	22	16.8	3	15	0	-	25	15.6				
Eclampsia	3	2.3	0	-	0	-	3	1.9	0.908			
GDM	2	1.5	0	-	0	-	2	1.3				
Anemia	1	0.8	0	-	0	-	1	0.6				

A total 90% of baby didn't had admission to NICU and only 10% of baby had admission to NICU.

There was no statistically significant difference found between NICU admission of baby and vitamin D level in mothers (Table 7).

A total 89.4% of babies didn't have any complication, 7.5% of babies had respiratory distress, 1.9% of babies had IUGR and 1.3% of babies had SGA.

There was no statistically significant difference found between neonatal complication and vitamin D level in mothers (Table 8).

Out of 160 subjects, 80.6% did not have any complication, 15.6% of subjects had PE, 1.9% of subjects

had eclampsia, 1.3% of subjects had GDM and 0.6% of subjects had anemia.

There was no statistically significant association found between maternal complication and vitamin D level (Table 9).

DISCUSSION

As the majority of female population residing in rural area of Kolar which comprises of women who are mostly housewives and spend most of their time indoors and are negligent towards antenatal care, hence risk of hypovitaminosis D is high, which was reported in this study. In this present study, majority (52.5%) of the study population belonged to the age group of 23-28 years and

85.6% were primigravida with 92.5% of the cases having a normal BMI of 18.5 to 24.99 kg/m^2 .

In the present study, majority (81.87%) of cases had vitamin D deficiency (serum vitamin D concentration of < 20 ng/dl) and 12.50% of cases had vitamin D insufficiency (20-29 ng/dl) and only 5.63% of cases had sufficient vitamin D levels of >30 ng/dl.

In a similar study done by Domaracki et al, in Polish women showed only 10.8% of cases had sufficient serum concentrations of 25(OH)D, while 43.7% had vitamin D deficiency and 45.6% had insufficient serum vitamin D levels.⁷

In another study done by Dawodu et al, in Qatar, a total of 47 (78%) mothers were vitamin D-deficient.⁸

In yet another study conducted on pregnant women in Thailand, the prevalence of hypovitaminosis D at delivery was 75.5%. Of these, 41.5% were vitamin D insufficient and vitamin D deficiency was found in 34.0% of women.⁹

In different study done in Beijing, China by Liu Y et al, they found that, of the total ninety-eight patient, there were twenty patients whose serum levels of total 25-OH vitamin D was lower than 50 nmol/L, which was considered as vitamin D deficiency.¹⁰

In another study done in Sweden by Lindqvist et al, the mean 25-OH vitamin D levels in women who underwent caesarean delivery due to suspected asphyxia was 43.6 ± 18 nmol/L, which was significantly lower than in controls (p = 0.04).¹¹

Amegah et al, observed in his study done in Ghana, that 83% of the study population had serum 25(OH)D levels < 75 nmol/l which was considered as vitamin D deficiency.⁴

These are a few studies done in different parts of the world and all these studies showed results comparable with this study. From this observation it is evident that population of both, tropical and non-tropical countries were largely vitamin D deficient.

Parity and vitamin D deficiency

In this study 85% of the study population were primigravida, but there was no statistically significant difference in serum vitamin D concentrations and parity. In a study by Sachan et al, also the study population had lower parity.⁵

Socioeconomic status

The study subjects were categorized into different socioeconomic class based upon modified BG Prasad classification. In this study, 62.5% of subject were in

lower middle class followed by middle class consisting of 18.8% of subject followed by 13.8% and 5% in lower class and upper middle class, respectively. It was observed that 72.5% of vitamin D deficiency subject were in lower middle class. 65.0 % of vitamin D insufficiency subject were in middle class. 77.8% of vitamin D sufficiency subject were in upper middle. There was a statistically significant difference (p=<0.001) found between socioeconomic status and vitamin D level.

In a similar study conducted by Rodriquez et al, in a South European population, higher risk of vitamin D deficiency was related to lower social class (RR = 1.94, 95% CI 1.19, 3.16) which was comparable to this study.¹²

Whereas in 2 other studies conducted by Pratumvinit et al and Veena et al, it was observed that maternal serum vitamin D levels were negatively associated with socioeconomic status and education level, which are not in agreement with the present study.^{9,13}

Mode of delivery

In this study, 80% of subject underwent LSCS and 20% of subject had vaginal delivery. Only 7.6% of vitamin D deficiency subject had vaginal delivery rest 92.4% of vitamin D deficiency subject underwent LSCS. Thus, there was a statistically significant association (p=<0.001) found between LSCS and vitamin D deficiency.

In a study by Lindqvist et al, it was seen that women who underwent emergency caesarean section due to suspected fetal asphyxia had lower vitamin D levels in pregnancy which was similar to this study results.¹¹

Baby birth weight and maternal vitamin D

In this study group of 160 newborn babies, 25 newborn babies were LBW (1.5-2.5 kg), 127 babies were 2.5-3.5 kg and eight babies were > 3.5 kg. All the mothers of 25 LBW babies had Vitamin D deficiency which was statistically significant (p = <0.001).

In 2 similar studies conducted by Bowyer et al, and Leffelaar et al, infants of mothers with 25-OH D deficiency during pregnancy had lower birth weight. These results were comparable with this study.^{14,15}

In a study by Domaracki et al, serum levels of 25(OH)D did not correlate significantly with neonatal birth weight, as opposed to the results of the present study.⁷

Neonatal complications

In the present study, there was no statistically significant association found between neonatal complication such as small for gestational age, low birth weight and respiratory destress with vitamin D level in mothers. In a study by Aghajafari et al, showed a significant association between small for gestational age infants and 25-OHD insufficiency compared with the comparison group, which is not according to this study results.¹⁶

In another study conducted by Ataseven et al, respiratory distress syndrome was more common with severe (28%) compared to mild-moderate 25(OH)D deficiency (14%) (p < 0.05).¹⁷

Maternal complications

In the present study 85.6% of subjects did not have any maternal complications and there was significant association seen between maternal complications like preeclampsia, eclampsia, GDM and anemia and serum vitamin D levels.

In the study of Domaracki et al, evident statistically significant differences (p=0.0021) in serum concentrations of 25(OH)D in women with PE and healthy controls were noted. Women with PE had vitamin D deficiency. This was not consistent with this study. But 25(OH)D was not identified as a significant predictor of GDM in this study, which was consistent with this study.⁷

In Mirzakhani et al, study women who had sufficient vitamin D levels (≥ 30 ng/ml) in early and late pregnancy had a significantly lower rate of preeclampsia compared with women with insufficient vitamin D levels (P = 0.04). This was not comparable to this results.¹⁸

In a study by Nicholas et al, they found no association between hypovitaminosis D (plasma levels of < 30 ng/ml) and preeclampsia, intrauterine growth restriction or gestational diabetes, which was consistent with this study results.⁶

CONCLUSION

In this study it was concluded that majority of subjects were vitamin D deficient and belonged to lower middle socioeconomic class. Majority of this subjects who underwent caesarean section were vitamin D deficient. Vitamin D deficiency was associated only with low birth weight of neonates and no other adverse obstetric outcome.

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